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(56) Documents Cited
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(54) Carrier base materials comprising hydroxypropylmethylcellulose and lecithin

(57) Tablets with a hydroxypropylmethylcellulose (HPMC) and lecithin carrier base have reduced friability and susceptibility to capping. The carrier base may also include dicalcium phosphate, magnesium stearate and/or micro-crystalline cellulose and is suitable for making vitamin tablets.

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The claims were filed later than the filing date within the period prescribed by Rule 25(1) of the Patents Rul s 1995

PATENTS ACT 1977

CAS/MNS/PP/A8683GB

Title: Carrier Base Material

Description of Invention

This invention relates to a carrier base material of the kind conventionally combined with one or more therapeutically active compounds, to form a solid dosage unit wherein the therapeutically active compound is gradually released from the solid dosage unit, and primarily but not exclusively, the invention relates to a carrier base material to be used as an excipient for one or more nutritional supplements.

Carrier base materials for use as excipients for therapeutic medicaments are well known, and numerous types are currently employed. A principal factor in the choice of an appropriate carrier base material is the rate at which the, for example, therapeutic compound, is released from the tablet once ingestion has occurred. Hydrogenated vegetable oil has in the past been an important component of such materials, providing such a favourable release rate, although recently this has become less popular, in view of increasing medical opinion suggesting links between such saturated fats and cardiovascular diseases.

A particularly suitable class of alternatives to hydrogenated vegetable oil as a primary component of carrier base materials has been found to be that comprising one or more hydroxy propyl methyl celluloses (HPMC's). By careful selection of the correct viscosity grade and relative proportion of the appropriate HPMC or combination of HPMC's, appropriate release rates may be obtained for the therapeutic compound "carried" by the base material.

In addition to such HPMC's, other compounds are conventionally used in such carrier base materials, such as lubricants to facilitate tablet forming, binders to increase hardness and reduce friability of a resulting tablet, and fillers to provide extra mass to tablets in order that the resulting tablet be of an acceptable size.

The above considerations apply equally where the therapeutic medicament is a nutritional supplement or vitamin composition. Such tablets, which may be complex and comprise several different active ingredients, often comprise one or more ingredients which are unsuitable for formation into tablets by direct compression.

Accordingly, a compressible carrier base material is necessary to reduce the inhibiting effect of these ingredients, such that tablets of sufficient strength and hardness may be produced without difficulty.

Specifically, studies by the applicants have shown that unacceptably high levels of conventional fillers and/or binders may be required in order for tableting to be effective, and for other desired properties of the resulting tablets, such as hardness, friability, and resistance to capping, to be obtained.

It is accordingly an object of the present invention to provide an improved carrier base material which overcomes/minimises the problems outlined above.

According to the invention, there is provided a carrier base material suitable for combination with a therapeutically active compound, to produce a solid dosage unit, wherein the carrier base material comprises hydroxy propyl methyl cellulose and a lecithin.

Preferably, the lecithin is a soya lecithin.

Conveniently, the lecithin is soya lecithin powder.

Preferably, the lecithin forms 1% to 10%, by weight of the solid dosage unit.

Conveniently, the lecithin forms 5% to 7% by weight of the solid dosage unit.

Preferably the hydroxy propyl methyl cellulose forms at least 6%, by weight, of the solid dosage unit.

Conveniently, the viscosity of the hydroxy propyl methyl cellulose is approximately 100,000 cps (centipoise).

Conveniently, the carrier base material further comprises dicalcium phosphate (anhydrous), and/or magnesium stearate, and/or micro-crystalline cellulose.

Preferably the therapeutically active compounds comprise nutritional supplements.

Conveniently, the therapeutically active compounds comprise one or more vitamin formulations.

The therapeutically active compounds may further comprise vitamin, mineral or other like compositions.

Preferably, the solid dosage unit is produced by direct compression.

There now follows a detailed description, by way of example only, of a preferred embodiment of the invention.

The following relates to a new carrier base material developed by the applicants for use in conjunction with multi-vitamin/nutritional supplement formulations. Such formulations are often relatively difficult to process into tablets, since several of the "ingredients" may be unsuitable for tableting, especially when formed under direct compression, a process whereby the components of the tablet are compressed without prior processing or granulation.

Accordingly, relatively high levels of fillers and binders are conventionally required to overcome these problems and to dilute the inhibiting effect of such non-compressible ingredients.

Dicalcium phosphate is a suitable such binder, and the applicants have found that the anhydrous form is particularly suitable for such purposes. The dihydrate is not used since the water of crystallisation associated therewith reduces the effective surface area available for binding, and thus more of the product is required, resulting in unacceptably large tablets.

The applicants have found that in the case of multi vitamin/nutritional supplement formulations, approximately 20% of anhydrous dicalcium phosphate, by weight of the solid dosage unit, provides sufficient binding.

Testing by the applicants has also shown that approximately 7% HPMC by weight of the solid dosage unit, is required to obtain a satisfactory release profile whereby approximately 70% of the active compounds are released after six hours from ingestion. The HPMC has a viscosity of 100,000 cps (centipoise) which together with the relative amount of HPMC used, determines the release profile.

The carrier base material comprises approximately 1.9% magnesium stearate by weight of the solid dosage unit, a lubricant known in the pharmaceutical industry and used to ensure that tablets, once pressed, do not stick to the moulds employed.

The carrier base material further comprises approximately 5.1% soya lecithin powder, a lecithin comprising approximately 96% or more by weight, phospholipids. Typically, soya lecithin powder comprises by weight,

Phosphatidylcholine	23.0%
Phosphatidylethanolamine	20.0%
Phosphatidylinositol	16.5%
Phosphatidylserine	2.5%
Phytoglycolipids	10.0%
Phosphatideacid	4.0%
Lysophosphatidylcholine	2.5%
Lysophosphatidylethanolamine	2.5%
Phytoserins and esters	2.0%
P-containing unknown lipids	9.5%
Sacharose	7.0%

The soya lecithin has the effect of significantly reducing the friability (resistance to crumbling) of resulting tablets when compared with an equal amount of dicalcium phosphate. Additionally, the hardness of the resulting tablet is seemingly unaffected by the lecithin addition, and the tablets' susceptibility to

capping (fracture along a plane substantially parallel to the face of the tablet) is also significantly reduced.

The applicants do not wish to limit the scope of this document by a full explanation of the link between the lecithin addition and the improved properties outlined above, although the applicants believe that the lecithin, by virtue of its "oily" nature renders the tablet less brittle than if dicalcium phosphate alone was employed as a binder. Analogies may be drawn between the nature of the lecithin and vegetable oil which has previously been employed as a timed release agent, although the applicants fully understand that there may be additional mechanistic explanations relating to the lecithin incorporation.

Accordingly, the incorporation of the lecithin in the above carrier base material, when used in conjunction with nutritional supplements and like products, provides unexpected improvements in friability level and susceptibility to capping, over components currently known, and by its nature, the lecithin is particularly suitable to "nutritional supplement" applications since it is neither a saturated fat, starch, sugar, or derived from an animal source.

The features disclosed in the foregoing description, or the following claims, or the accompanying drawings, expressed in their specific forms or in terms of a means for performing the disclosed function, or a method or process for attaining the disclosed result, as appropriate, may, separately or in any combination of such features, be utilised for realising the invention in diverse forms thereof.

CLAIMS:

1. A carrier base material suitable for combination with one or more therapeutically active compounds, to produce a solid dosage unit, wherein the carrier base material comprises hydroxy propyl methyl cellulose and a lecithin.

2. A carrier base material according to Claim 1 wherein the lecithin is a soya lecithin.

3. A carrier base material according to Claim 2 wherein the lecithin is a soya lecithin powder.

4. A carrier base material according to any one of claims 1 to 3 wherein the lecithin forms 1% to 10% by weight of the solid dosage unit.

5. A carrier base material according to any one of claims 1 to 4 wherein the lecithin forms 5% to 7% by weight of the solid dosage unit.

6. A carrier base material according to any one of the preceding claims wherein the hydroxy propyl methyl cellulose forms at least 6% by weight, of the solid dosage unit.

7. A carrier base material according to any one of the preceding claims wherein the viscosity of the hydroxy propyl methyl cellulose is approximately 100,000 cps (centipoise).

8. A carrier base material according to any one of the preceding claims further comprising anhydrous dicalcium phosphate.

9. A carrier base material according to any one of the preceding claims further comprising magnesium stearate.

10. A carrier base material according to any one of the preceding claims further comprising micro-crystalline cellulose.

11. A carrier base material according to any one of the preceding claims wherein the or each therapeutically active compound comprises nutritional supplements.

12. A carrier base material according to any one of the preceding claims wherein the or each therapeutically active compound comprises one or more vitamin formulations.

13. A carrier base material according to any one of the preceding claims wherein the or each therapeutically active compound comprises mineral compositions.

14. A carrier base material according to any one of the preceding claims wherein the solid dosage unit is produced by direct compression.

15. A carrier base material according to any one of claims 8 to 14 comprising 20%, by weight of the solid dosage unit, of anhydrous dicalcium phosphate.

16. A carrier base material according to any one of the preceding claims wherein, in use, approximately 70% of the or each active compound is released within 6 hours from ingestion.

17. A carrier base material according to any one of claims 9 to 16 comprising approximately 1.9% magnesium stearate by weight of the solid dosage unit.

18. A carrier base material substantially as hereinbefore described.

19. Any novel feature or novel combination of features described herein.

The Patent Office

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Application No: GB 9519838.8
Claims searched: 1 to 18

Examiner: Mr S J Pilling
Date of search: 20 December 1996

Patents Act 1977
Search Report under Section 17

Databases searched:

UK Patent Office collections, including GB, EP, WO & US patent specifications, in:

UK Cl (Ed.O): A5B (BJC)

Int Cl (Ed.6): A61K 9/20, 47/00, 47/18, 47/38

Other: ONLINE: CAS ONLINE, WPI

Documents considered to be relevant:

Category	Identity of document and relevant passage		Relevant to claims
X	EP 0497162 A1	(ALFA WASSERMAN) see page 3 lines 55 to 57, Examples 5, 8 and 9.	1-3, 6,7,9,14, 16
X	US 4374082	(HOCHSCHILD) see the example and column 4 lines 23 to 26.	1-3,11,12
X	US 4332789	(MLODOZENIEC) see Examples I, III and IV, column 34 lines 28 to 29 and Claim 1.	1,2,4,6,7, 11-13

X	Document indicating lack of novelty or inventive step	A	Document indicating technological background and/or state of the art.
Y	Document indicating lack of inventive step if combined with one or more other documents of same category.	P	Document published on or after the declared priority date but before the filing date of this invention.
&	Member of the same patent family	E	Patent document published on or after, but with priority date earlier than, the filing date of this application.